

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

5,500

Open access books available

136,000

International authors and editors

170M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



Uses of the Response Surface Methodology for the Optimization of Agro-Industrial Processes

*José Manuel Pais-Chanfrau, Jimmy Núñez-Pérez,
Rosario del Carmen Espin-Valladares,
Marco Vinicio Lara-Fiallos and Luis Enrique Trujillo-Toledo*

Abstract

Response surface methodology is a tool for the design of experiments, widely used today to optimize industrial processes, including agro-industrial ones. Since its appearance in the last century's fifties, hundreds of articles, chapters of books, and books attest to this. In this work, a general overview of this tool's general practical aspects is made. This statistical tool's usefulness and popularity, used in the optimization of agro-industrial processes and in making them more efficient and sustainable, is described through multiple examples.

Keywords: response surface methodology, agro-industry, central composite design, independent variables, uncontrolled variables, response variables, optimization

1. Introduction

The response surfaces methodology (RSM) is a set of statistical tools for the design of experiments aimed at finding the value or values of the independent variables, which allow developed, improved and optimization (i.e., finding the maximum, minimum, or equal to a certain convenient value) one or more dependent variables or responses [1, 2].

Since the first works reported by Box and coworkers [3–5], RSM has been gaining popularity among researchers, developers, and engineers, and today it has become one of the preferred tools for increasing the productivity and efficiency of R&D processes and the production of goods and services.

The agro-industry, on the other hand, comprises a set of process industries that use agricultural and livestock resources to transform them into products of higher added value. Processed and improved foods, nutraceutical foods and beverages, chemical products and bioactive substances for the chemical, pharmaceutical and cosmetic industries, industrial enzymes and above all, vast and abundant quantities of plant and animal biomass, which could be the primary renewable raw materials with which that will count the industry of the future, are some of the main “outputs” of the agro-Industry.

By their nature, the sources of the raw materials of the agro-industry are renewable and could be a strategical industrial sector for the sustainable development

of the whole of humankind, given the constant growth of the human population, Ambiental deterioration, and the evident depletion of the natural sources of raw materials. It is for this reason, that it is required to have well-designed processes that generate a minimum negative impact on the already deteriorated ecosystems, and in which yields, and productivity are maximized.

The objective of this work is to show, through a group of examples, the utility of RSM for the design of efficient, productive agro-industrial processes with a minimum negative impact on agro-ecosystems.

2. Agro-industries: the pillar in sustainable development that the world needs

Agroindustry can be defined as the process industries that use agricultural, live-stock and aquaculture products as raw materials, transforming them into valuable, more elaborate products with greater added value. Among the products emerging from agroindustries are processed foods and beverages, dry and canned foods with greater durability, fermented foods and beverages with nutraceutical properties, as well as basic chemicals, precursors of other chemical compounds, biofuels, industrial enzymes, bioactive products, such as antibiotics, probiotics, prebiotics and synbiotics substances, vitamins, organic acids, phytohormones, antioxidant agents, growth factors, etc. (Figure 1).

Agro-industries can be subdivided into primary, secondary and tertiary transformation agroindustries, depending on the set of predominant operations carried out in them and the degree of complexity of their output products (Figure 1).

In primary transformation, the selection, crushing, separation, isolation, concentration, or drying of the product or products of interest usually predominate. The sugar factories made from sugar cane or sugar beet [6], the traditional dairy industry where milk is powdered, evaporated, or condensed (whole, defatted or lactose-free) [7], or the slaughter of cattle meat [8] or industries that produce concentrated juices or condiments and canned foods are examples of industries where these operations of physicochemical transformation of raw materials from agriculture, aquaculture and livestock, into products prevail.

On the other hand, in secondary transformation agro-industries, the products, by-products and residuals of the first transformation are usually used as starting

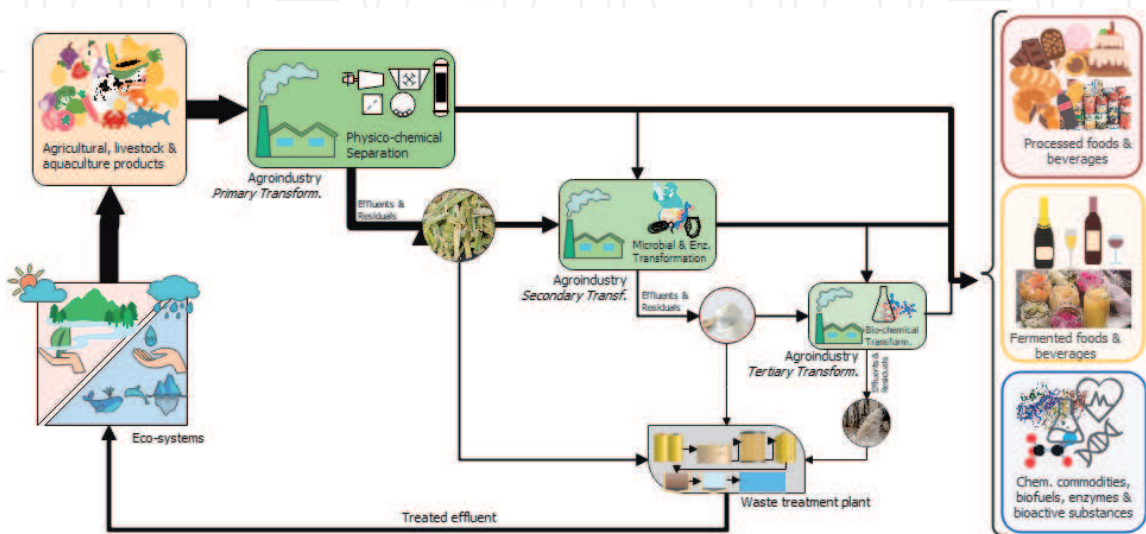


Figure 1.
Agroindustry: Its source of raw materials and main productions.

raw materials, and in their transformation performed by microorganisms, perfectly adapted to grow and develop using these raw materials, obtaining, as a result of their microbial activity, fermented products and beverages, with beneficial nutritional and food properties. Fermented food and beverage production industries [9, 10], such as yoghurt [11, 12], kefir [13, 14] and the manufacturing of beer [15] and wine [16], fermented sauces and condiments, such as soy sauce, as well as the production of bio-ethanol [17, 18], vinegar [19, 20] and some organic acids [21, 22], such as citric acid [23] and lactic acid [24], are practical examples of these agro-industries, where microorganisms and enzymes carry out the transformation of raw materials to product.

Finally, in the tertiary transformation agro-industries, the products, by-products or residues of the primary and secondary transformation agro-industries continue to be transformed chemically and/or biochemically into new chemical compounds, like bioactive compounds, enzymes, polysaccharides, gums, phytohormones, growth factors, etc. These, as a rule, are the products derived from agro-industries that have the highest added value. Some industrial enzymes such as cellulases [25], lipases [26] amylases [27], fructosyltransferases and invertases [28]; macromolecules like fructo- and galactooligosaccharides (FOS and GOS) [29–31], etc., are examples of agro-industries of tertiary transformation.

Currently, the production volumes of tertiary transformation agro-industries are significantly lower than the previous two. However, they should increase in the future, stimulated by the high prices of these products and the depletion of oil, the main raw material from which the traditional chemical industry's precursors are obtained [32].

An agro-industrial process can be considered as a set of operations that allow the gradual transformation of the process inputs (for example, raw materials, material, and energy resources) into the outputs (such as the main product (s), by-products, disposable materials and waste) (**Figure 2**).

As a rule, the added value of the product or products is significantly higher than the value of the inputs and other elements of the outputs.

An agro-industrial process, like any other, is made up of a series of stages of transformation processes. Each stage can be made up of one or more unit operations. In each of the stages of the transformation process of raw materials or intermediate products, a set of factors or variables can influence the efficiency and speed of said transformation. These factors can be subdivided into controllable and non-controllable factors or variables (**Figure 3**). The first ones are all those intensive variables of the process (such as temperature, pH, the concentration of certain analyte, etc.), whose values must be kept within a certain range on any scale and which, besides, are the ones that have the real possibility of being controlled within pre-established ranges in

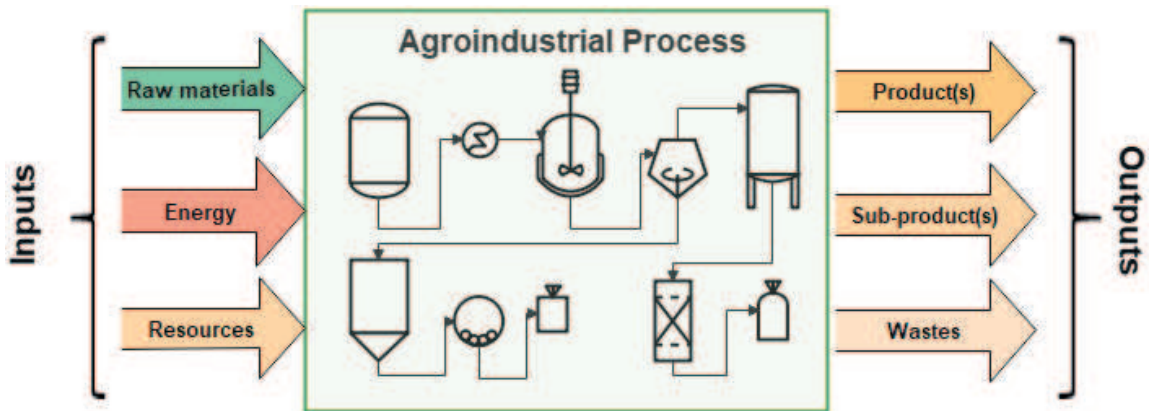


Figure 2.
General scheme of an agro-industrial process.

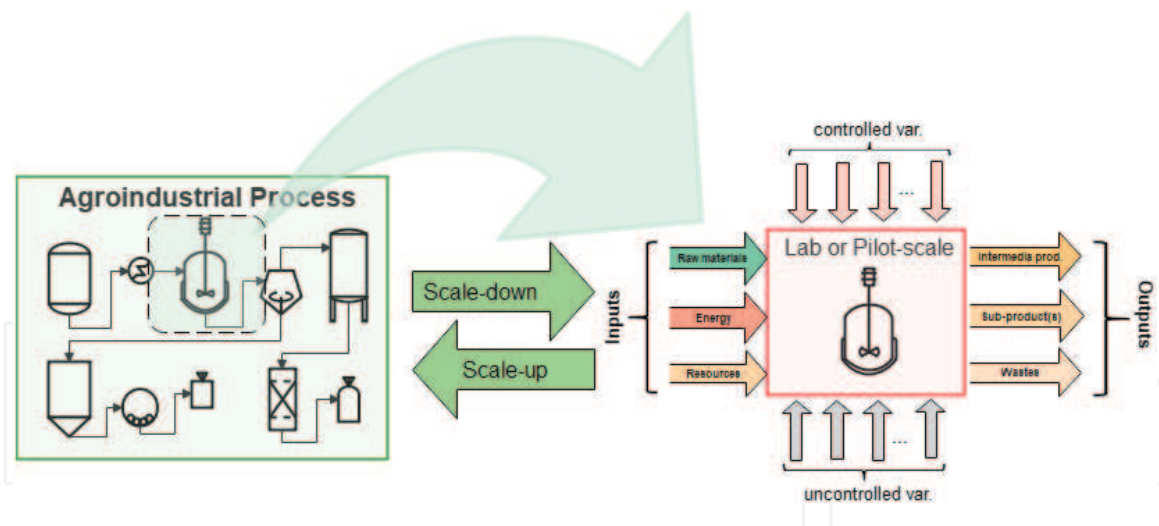


Figure 3.

The two ways to optimise agro-industrial processes: Scale-down of established processes and the Scale-up of new processes.

the different scales. The second, for their part, are all those variables, including those whose existence is still unknown, that may influence the transformation process but are not within reach of the processes and technologies to be controlled. By focusing attention on the intensive controllable variables, not only will it be possible to find the combination of these that allow the development of an optimal transformation process, but it will also allow knowing the values that must be achieved in the productive scale of a certain variable or response factor, commonly associated with some quality attribute of the final or intermediate product within the process.

An efficient and sustainable agro-industrial process will *maximize* the efficiency of the transformation of raw materials to finished products, *minimizing*, at the same time, the use of energy resources and the generation of by-products disposable and residual materials. The latter can be achieved by optimizing each of the stages of the process.

To do this, normally, you can proceed in two ways. If it is intended to optimize an already established large-scale non-optimal process, the established process could be scale-down to a smaller scale, a pilot-scale for example, or later to a laboratory, where all the necessary optimization experiments could be developed (**Figure 3**).

If it is intended to optimize the design of new processes, these can be optimized on a laboratory scale, first and later, these optimized processes would be scaled-up to pilot and further to industrial scale.

Due to the wide range of useful products that emerge from the agro-industry, ranging from products that improve the durability, texture and nutritional composition of natural foods, through simple chemical substances, precursors of other more complex and elaborated, to complex substances like antibiotics, prebiotics, hormones, enzymes, polysaccharides, etc. (**Figure 1**). There are numerous niches where modern techniques of experiment design and process optimization can be used [33, 34].

Among the most popular and effective tools to know the optimal parameters of a process is the response surface methodology (RSM), frequently associated with searching for an extreme value of one or more objective functions. The objective function or response is frequently associated with one or more of the product's attributes of a stage or unit operation of the process (for example, the concentration, the yield, the efficiency, the conversion, the productivity, etc.). Additionally, there may be other objective functions or responses, which can also integrate into the same optimization process, which may be related to other needs of the unit process or stage, such as the reduction of some by-product or residue, the decrease in consumption of energy, cleaning agents, shortening of the processing time, etc. In such cases, we would be in the presence of multi-objective optimization.

3. A short overview of response surface methodology (RSM)

The idea of the RSM is, through the design of experiments, to find the relationship between a certain response variable, commonly associated with one of the attributes of the experimental unit's output product with a few controllable variables. Strictly speaking, any response variable depends on both controllable and non-controllable variables. However, it is necessary to try to find a certain objective function, dependent only on a few controllable variables (usually from two to six), which allows navigating its surface in search of the combination of controlled variables with which an extreme value of the objective function is reached.

The response variable, as mentioned before, will also depend on the contribution of a certain "noise" function that depends on the rest of the controllable variables not taken into account in the objective function, as well as on the non-controllable factors. Still, it must seek that noise's influence on the response is low enough or not significant. The determining influence on the response can be exerted mainly by the contribution of the objective function (**Figure 4A**).

To find the relationship between the variable response and the independent variables or controllable factors requires careful design of the experiments. These experiments must be carried out randomly and making the necessary replications to have the necessary certainty of their results [35]. In this sense, first of all, there must be solid evidence that the independent variables to be evaluated significantly influence the response variable or variables under study. This is based on our own experiments previously carried out or abundant reports published in the scientific literature. And secondly, must choose a suitable range for the independent variable analyzed, neither too narrow nor too long, so that the different values obtained from the response variable are notable.

The experimental runs must be carried out so that they cover the entire possible range of the independent variables that are being evaluated in the best way. Thus, the influence that each one, separately and combined with other independent variables, exerts on the response variables being analyzed can be evaluated. This can be ensured when the total sum of the products of all the coded independent variables of each run is equal to zero. The latter is known as the *orthogonal* design of experiments.

In addition to randomization and to minimize the influence that uncontrolled factors or variables may exert on the response variables, the different treatments are usually grouped into experimental blocks [36]. The latter can be beneficial, especially when various factors are evaluated, and the experiments must be performed over several days (**Figure 4B**).

In this way, the experiments must be *random*, with *replications* and designed in an *orthogonal* and *block-based* manner [37].

The most common experiment designs used in response surface methodology are the central composite design (CCD) and the Box–Behnken design (BBD). As a rule, in the BBDs, there are fewer experimental runs than in the CCDs (three levels for each factor in BBD, against five levels in CCD, for example). Therefore, it may be the preferred choice when the experiments are costly or when you need to have resulted in a shorter time. However, more robust and reliable models are obtained in CCDs, and they better support the loss or mismeasured response of the runs. The latter makes CCDs the "workhorse" and the first choice of researchers trying to optimize agro-industrial processes [37].

Fortunately, statistical packages accurately plan these experiment designs. Commercial statistical software such as Design-Expert®, JMP®, and Minitab® stand out, which are very useful and popular among scientific researchers and engineers communities. Additionally, there are becoming more popular every day; some free tools, such as the R and Python languages, are somewhat more

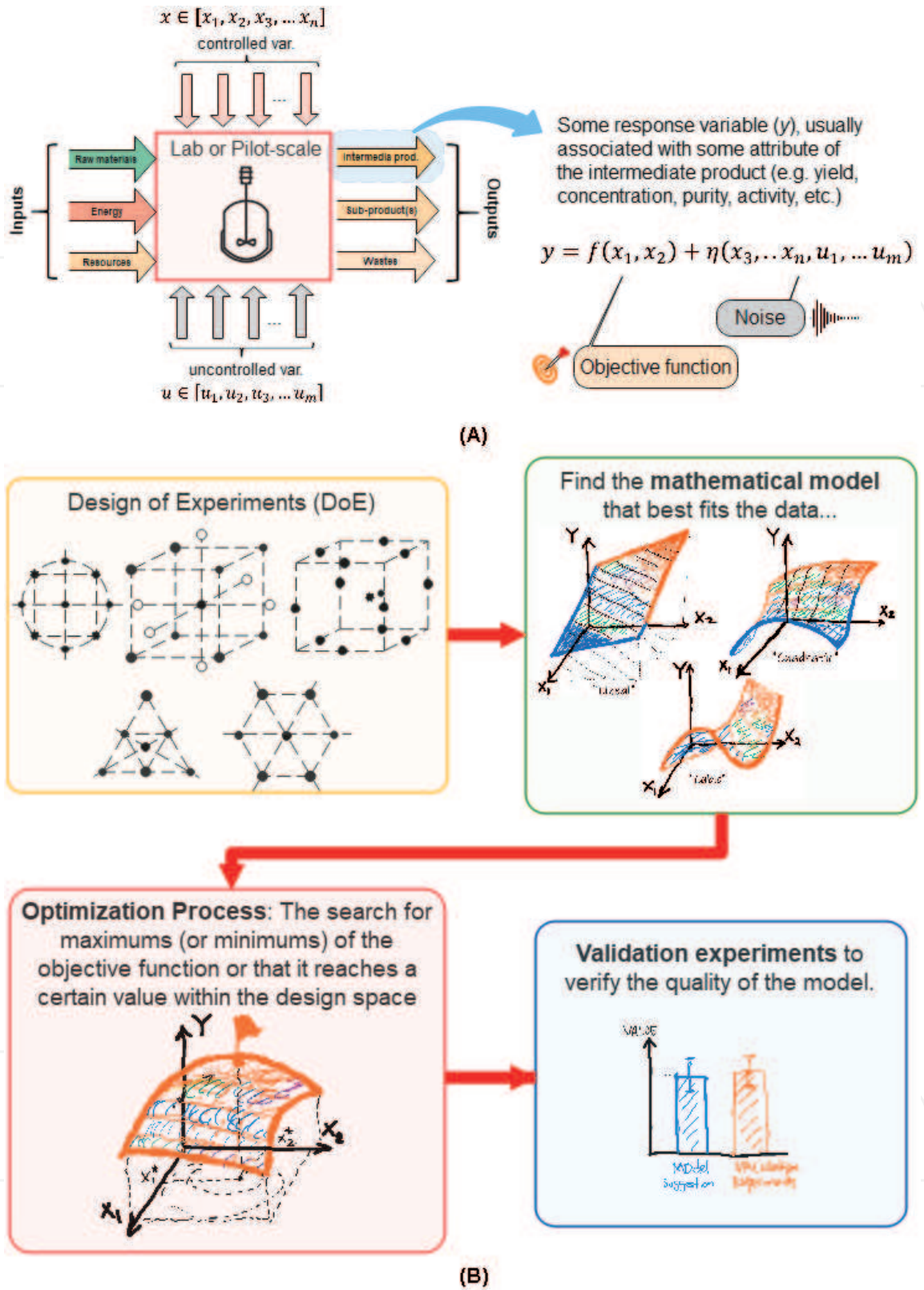


Figure 4.
(A) The response variable and its links with objective functions and noise, (B) general workflow for implementing response surface methodology.

complex to use and require greater statistical and programming knowledge for their successful use.

Once the experiments have been designed and executed, it is necessary to adjust the experimental data to a certain function that represents a close approximation to the response variable or variables obtained to each treatment, depending on the experiments' independent variables or factors (**Figure 4B**).

Depending on the values obtained in the response variable's experiments and if the difference between the maximum and minimum values obtained is huge, it will be necessary to transform the response variable before finding the adjustment function. Frequently the response variable (s), transformed or not, are adjusted to a certain polynomial, depending on the chosen design.

Subsequently, the polynomial that best fits the experimental data will be chosen. An analysis of variance will be carried out to the chosen polynomial. Those coefficients that are not significant for the model will be discarded as long as they do not sacrifice different runs' orthogonality. The quality of the model is evidenced through different statistical parameters, such as the adjusted quadratic coefficient of regression, adequate precision, the graphs of the predicted value versus the real value or through the graphs of the distribution of the residuals; the model may or may not be used, to find, within the design space of the independent variables, the optimal values of the function that adjusts the response variable(s) with the independent variables.

Once the appropriate model has been chosen, it is proceeding to explore the extreme or optimal values of the response function within the design space, that is, to find the combination of independent variables or factors that make the response objective function reach its maximum value, minimum value or equal to a specific value, depending on the response function. During the response function's optimisation process, and depending on the model's precision and variance, one or more extreme values may appear. If the extreme values found are related to variables or independent factors that are not related or are very far from each other, new experiments may be necessary around these points to improve the model's precision (**Figure 4B**).

On the contrary, if within the explored design space there is a single extreme value or only a few within a close region of the independent variables, can choose this solitary extreme value or can select one representative of the set of comparable response values can be chosen to proceed with a group of model confirmation or validation experiments.

There is no hard and fast rule about how many of these validation experiments are necessary, but they are usually between three and five. The model is validated when all the response function values are located within the range predicted by the model. The average weight of these does not differ significantly ($p < 0.05$) from the value predicted by the model. Otherwise, it would be suggesting that the model does not have the necessary accuracy. It is essential to continue exploring the search for extreme values within or outside of the original design space. In the latter case, an additional set of RSM-experiments would need to achieve (**Figure 4B**).

4. Agroindustry: a suitable receptor for the use of the response surface methodology (RSM)

Since Box and Wilson in 1951 [3] proposed this methodology, hundreds of scientific articles have been published [38–41].

Due to the wide range of useful products that emerge from the agro-industry, ranging from products that improve the durability, texture and nutritional composition of natural foods, through simple chemical substances, precursors of other more complex and elaborated, to complex substances like antibiotics, hormones, enzymes, polysaccharides, etc. (**Figure 2**). There are numerous niches where modern techniques of experiment design and process optimization can be used [42, 43].

Among the most popular and effective tools to know the optimal parameters of a process is the response surface methodology, frequently associated with development of new products [44–46] and processes [47, 48], the maximization of the productivity or yield of the process products [49–52], the reduction of their

Title	Clase ¹	Source/Product	RSM DOE	Optimal values	Ref.
Control of selected fermentation indices by statistically designed experiments in industrial scale beer fermentation.	AI PT	Optimization of beer fermentation	Box–Behnken	Pitching rate 6·10 ⁶ cells/mL; fermentation temp. 11.2 °C; aeration level 10.5 mg/L; and CCTs filling time 13.5 h.	[57]
Effect of ohmic heating on quality and storability of sugarcane juice.	AI PT	Sugarcane juice/sugarcane juice	Box–Behnken	Ohmic heating of sugarcane juice at 70°C for 3 min holding time.	[58]
Extraction of steviol glycosides from dried <i>Stevia rebaudiana</i> by pressurized hot water extraction.	AI PT	<i>Stevia rebaudiana</i> Bertoni leaves/Stevioside	CCD	2 bars of pressure, 20 min reaction time, and 20% dry leaves to water ratio	[59]
Optimization of spray-drying parameters for the production of ‘Cempedak’ (<i>Artocarpus integer</i>) fruit powder.	AI PT	Fruit juice/fruit powder	CCD	Air temperature of 160°C and maltodextrin conc. of 15% (w/w)	[60]
Optimizing the extraction of bioactive compounds from pu-erh tea (<i>Camellia sinensis</i> var. <i>assamica</i>) and evaluation of antioxidant, cytotoxic, antimicrobial, antihemolytic, and inhibition of α -amylase and α -glucosidase activities.	AI PT	Pu-erh tea/Antioxidants	CCD	Temperature of 85.4°C and time of 3 min	[61]
Maize stover as a feedstock for enhanced laccase production by two gammaproteobacteria: A solution to agroindustrial waste stockpiling.	AI PT	Maize stover/laccase	Box–Behnken	pH 5, 0.50 g biomaterial, 100 rpm and 0.10 NaNO ₃	[62]
Evaluation of textural properties of corn based extruded products.	AI PT	Three corn varieties/Extruded product	Box–Behnken	Temperature: 127.66°C, 18.96% feed moisture and 92:4:4 feed composition	[63]
Response Surface Methodology approach for optimization of endoglucanase from alkaliphilic <i>Fusarium oxysporum</i> VSTPDK and its potential application in pulp and paper industry.	AI PT	Rice straw/CMCase	CCD	pH 8.5, temperature 45°C, ammonium sulphate concentration 3% and 8 day incubation.	[64]
Antioxidant and prebiotic effects of a beverage composed by tropical fruits and yacon in alloxan-induced diabetic rats.	AI PT	Yacon extract + fruit juice/fructo-oligosaccharides	CCD	Yacon extract: 50% and sweetener: 0.07%	[65]
Optimization of concentrating process using rotary vacuum evaporation for pineapple juice.	AI PT	Pineapple juice/concentrated juice	CCD	Temp. 60°C and pressure 200 mBar for 75 min.	[66]

Title	Clase ¹	Source/Product	RSM DOE	Optimal values	Ref.
Pre-treatment optimization of barley straw as agro-industrial waste via alkaline peroxide and ultrasound for soluble sugar production and degradation.	AI PT	Barley straw/Sugars	Box–Behnken	US Power: 20 kj/kg DM Particle size: 0.6 mm	[67]
Techno-economic feasibility of bioethanol production via biorefinery of olive tree prunings (OTP): Optimization of the pretreatment stage.	AI PT	OTP/bioethanol	Box–Behnken	Minimum of Total Capital Cost: Temp. 199.98°C, 8 g H ₂ SO ₄ /100 g; 35% (w/v)	[68]
Design of experiments for enhanced production of bioactive exopolysaccharides from indigenous probiotic lactic acid bacteria.	AI ST	Lactose/ Exo-polysaccharides	Box–Behnken	<i>Enterococcus faecium</i> K1: Lactose: 10.07g/L, Ammonium citrate 2.48 g/L, pH 5.4	[69]
Response surface methodology to optimize a bioprocess for kefir production.	AI ST	WP/kefir	CCD	Temp.: 25°C and 44.1% (w/w) of WP	[70]
Microwave-assisted extraction of pectin from “Saba” banana peel waste: Optimization, characterization, and rheology study.	AI ST	Banana peel waste/pectin	CCD	195° C, 8% solid–liquid ratio, and pH 3 HCl	[71]
Hydrolysis of orange peel with cellulase and pectinase to produce bacterial cellulose using <i>Gluconacetobacter xylinus</i> .	AI ST	Orange peel/cellulose	Box–Behnken	cellulase of 1589.41 U/g, pectinase of 31.75 U/g and a reaction time of 5.28 h	[72]
Valorization of sugarcane bagasse to high value-added xylooligosaccharides and evaluation of their prebiotic function in a synbiotic pomegranate juice	AI ST	Sugarcane bagasse/xylan	CCD	5.63% H ₂ O ₂ , 12.91% NaOH, and extraction time of 17.51 h	[50]
Playing with the senses: application of Box–Behnken design to optimize the bukayo formulation.	AI ST	Coconut meat and juice+sugar/bukayo acceptability	Box–Behnken	430 g young coconut meat, 400 g sinakob, and 340 g coconut juice	[73]
Utilization of Atlantic salmon by-product oil for omega-3 fatty acids rich 2-monoacylglycerol production: Optimization of enzymatic reaction parameters.	AI ST	Salmon By-product Oil/ Omega-3	Box–Behnken	Reaction temp. 42.5°C, time 4.15 h, enzyme load 42.81%, & ethanol: oil mol. Ratio 49.82	[74]
Bioconversion of cheese whey permeate into fungal oil by <i>Mucor circinelloides</i> .	AI ST	Whey permeate/fungal oil	CCD	Fermentation temp. 33.6°C and pH 4.5	[75]
Olive mill and winery wastes as viable sources of bioactive compounds: A study on polyphenols recovery.	AI ST	olive pomace residues/ polyphenols	Box–Behnken	Olive pomace microwave-extraction: ethanol:water 50:50 (v/v), 90°C, 5 min	[76]

Title	Clase ¹	Source/Product	RSM DOE	Optimal values	Ref.
Development of a low-temperature and high-performance green extraction process for the recovery of polyphenolic phytochemicals from waste potato peels using hydroxypropyl β -cyclodextrin.	AI ST	Potato peel/polyphenols	Box–Behnken	pH 5.0, ratio solvent-to-dry weight 80 mL g ⁻¹ and agitation speed 800 rpm	[77]
Optimized preparation of activated carbon from coconut shell and municipal sludge.	AI ST	Coconut shell/activated carbon	Box–Behnken	Temp.: 800°C, activation time: 60 min, activator concentration: 2.5 mol/L, a 50% coconut shell.	[78]
Response surface methodology as a tool for modeling galacto-oligosaccharide (GOS) production.	AI ST	DWP/GOS	CCD	DWP: 18 g/ml, 0.20 g/L of β -galactosidase	[79]
Optimization of β -galactosidase production by batch cultures of <i>Lactobacillus leichmannii</i> 313 (ATCC 7830 TM).	AI ST	Lactose/ β -galactosidase	CCD	pH 7.06 and 15.3 g/L lactose	[80]
An eco-friendly pressure liquid extraction method to recover anthocyanins from broken black bean hulls.	AI ST	Broken black bean hulls/anthocyanins	Box–Behnken	Ratio ethanol and citric acid sol.n 0.1 mol/L of 30:70 (v/v), flow rate: 4 mL/min, 60°C.	[81]
Canola meal as a promising source of fermentable sugars: Potential of the <i>Penicillium glabrum</i> crude extract for biomass hydrolysis.	AI ST	Canola meal/ β -glucosidase	CCD	Fermentation time: 6.5 days, pH adjusted to 6.0, and substrate concentration of 2%	[82]
Optimization of galacto-oligosaccharides (GOS) synthesis using response surface methodology.	AI ST	Lactose/GOS	CCD	Lactose conc. of 400 g/l, enzyme conc. of 13.5 g/l and reaction time of 13 min	[83]
Pre-treatment of sugarcane bagasse with aqueous ammonia–glycerol mixtures to enhance enzymatic saccharification and recovery of ammonia.	AI ST	Sugarcane bagasse/Sugars	Box–Behnken	Conc. of ammonia: 9.25%, pre-treatment time: 1.86 h, pre-treatment temp.: 180°C	[84]
Low-cost production of PHA using cashew apple (<i>Anacardium occidentale</i> L.) juice as potential substrate: optimization and characterization.	AI ST	Cashew apple juice/PHA	CCD	Conc. of total reducing sugar of 50 g/L, inoculum of 50 mL/L, and urea of 3 g/L.	[85]
A facile noncatalytic methyl ester production from waste chicken tallow (WCT) using single step subcritical methanol: Optimization study.	AI ST	WCT/biodiesel (FAME)	CCD	167°C, 36.8 min., and 42.7:1 (methanol/WCT, mol/mol)	[86]

Title	Clase ¹	Source/Product	RSM DOE	Optimal values	Ref.
Recovery and bio-potentialities of astaxanthin-rich oil from shrimp (<i>Penaeus monodon</i>) waste and mackerel (<i>Scomberomous niphonius</i>) skin using concurrent supercritical CO ₂ extraction.	AI ST	Astaxanthin-rich oil/shrimp waste & fish skin	CCD	Extraction temp. 45.7°C; pressure 264.09 bar, and shrimp waste-to-fish skin mixing ratio 79.63:20.37.	[87]
Zero-waste biorefinery of oleaginous microalgae as promising sources of biofuels and biochemicals through direct transesterification and acid hydrolysis.	AI ST/ TT	Microalgae (marine <i>Chlorella</i> sp.)/biofuels (FAME) & sugars.	Box–Behnken	FAME yield: Temp. 70 °C, ratio of chloroform:methanol 1.35:1 and reaction time 120 min. Sugar yield: 7.5% H ₂ SO ₄ , 60 min hydrolysis time, 3% biomass loading, and 100°C hydrolysis temp.	[88]
Sequential production of lignin, fatty acid methyl esters and biogas from spent coffee grounds (SCG) via an integrated physicochemical and biological process.	AI TT	SCG/Lignin/FAME & biogas	CCD	Temp. 161.0°C, sulfuric acid: 3.6% and methanol:SCG ratio: 4.7 mL/g	[89]
Heterogeneous catalytic conversion of rapeseed oil to methyl esters: Optimization and kinetic study.	AI TT	Rapeseed oil/FAME	CCD	Catalyst ratio (bentonite/NaOH): 1:20; catalyst amount: 6%wt.; reaction time: 3.5 h.	[90]
Abbreviations: DWP: demineralised whey powder; WP: whey powder; CMCase: carboxy-methyl-celulase; PHA: poly-hydroxy-alkanoate; FAME: fatty-acid methyl-ester. ¹ AI PT, ST, TT: Agro-industry (AI) of primary, secondary, or tertiary transformations.					

Table 1.
Some of the recent work on the response surface methodology related to the agro-industry.

production costs [53], the minimization of risks for the human health [54] or its negative impacts on ecosystems [55, 56].

A summarized sample of some of the recent work in agro-industry related to the response surface methodology is shown in **Table 1**.

Table 1 shows more than thirty selected examples chosen from the last five years (2017–2021) from the multiple reports in the specialized bibliography, using RSM in all areas of agro-industry. In the selected cases, it is confirmed that the BBD and CCD designs are the most widely used and the utility that these experimental design and optimisation tools provide to researchers and engineers working in the agro-industry is demonstrated.

On the other hand, RSM is conveniently intertwined with the concepts of the “circular economy” [91] applied to agro-industry toward a broader framework of a sustainable bioeconomy [92, 93], where it is intended to maximize the efficiency and productivity of the transformation processes of raw materials into products, with a minimal negative impact on the environment and to minimize generation of by-products, wastes, and residuals of the agro-industrial processes, and, at the same time, reuse the latter as sources of raw materials for other products, valuing them.

On some occasions the by-products and wastes of some agro-industrial processes become sources of raw materials for obtaining other valuable products through chemical, enzymatic or biological transformation. Some examples such as whey, a by-product of the cheese industry [94–96], and molasses and bagasse by-products of the sugar cane industry, from which some valuable products are obtained [97–100].

This fact gives rise to the concept of biorefineries and circular economies [91, 93], applicable in certain economic agricultural crops exploited on a large scale, where a group of valuable products could be obtained from abundant and renewable raw materials, in addition to those that have traditionally been obtained previously.

5. Conclusion

Despite an appreciable decrease in publications related to the response surface methodology in agro-industry, in 2020 and so far in 2021, due to the effects of the impact of the SARS-CoV-2 pandemic in the world, everything indicates that RSM is a prevalent tool among researchers and engineers to improve agro-industrial processes, as demonstrated in this work, and that it will continue to be very useful and necessary to achieve efficient, sustainable and friendly agro-industrial processes with the environment. For this reason, once the effects of the pandemic have passed, new reports of applications of the use of this statistical tool will surely continue to appear.

Acknowledgements

We wish to express our gratitude to the authorities of the **Universidad Técnica del Norte** (UTN, Ibarra, Imbabura, Ecuador) for their unconditional support, and to **Dr. Bolívar Batallas** and **Dr. Hernán Cadenas**, Dean and Vice-Dean of our Faculty, respectively, for their support for this publication.

IntechOpen

Author details

José Manuel Pais-Chanfrau^{1*}, Jimmy Núñez-Pérez¹,
Rosario del Carmen Espin-Valladares¹, Marco Vinicio Lara-Fiallos¹
and Luis Enrique Trujillo-Toledo²

1 North-Technical University (Universidad Técnica del Norte, UTN), FICAYA,
Ibarra, Imbabura, Ecuador

2 University of the Armed Forces (Universidad de las Fuerzas Armadas, ESPE),
Quito, Pichincha, Ecuador

*Address all correspondence to: jmpais@utn.edu.ec

IntechOpen

© 2021 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. 

References

- [1] Myers R, Montgomery D, Anderson-Cook C. Response Surface Methodology: Process and Product Optimization Using Designed Experiments. 4th ed. Wiley Series in Probability and Statistics. Hoboken, New Jersey: John Wiley & Sons, Inc; 2016. 854 p. DOI: 10.1017/CBO9781107415324.004
- [2] Khuri AI. Response Surface Methodology and Its Applications In Agricultural and Food Sciences. *Biometrics Biostat Int J*. 2017;5(5): 155-63. Available from: <https://medcraveonline.com/BBIJ/BBIJ-05-00141.pdf>
- [3] Box GEP, Wilson KB. On the Experimental Attainment of Optimum Conditions. *J R Stat Soc Ser B*. 1951;13: 1-38. DOI: 10.1111/j.2517-6161.1951.tb00067.x
- [4] Box GEP, Hunter JS. Multi-Factor Experimental Designs for Exploring Response Surfaces. *Ann Math Stat*. 1957;28:195-241. DOI: 10.1214/aoms/1177707047
- [5] Box GEP, Draper NR. A Basis for the Selection of a Response Surface Design. *J Am Stat Assoc*. 1959;54:622-54. DOI: 10.1080/01621459.1959.10501525
- [6] van der Poel P, Schiweck H, Schwartz T. Sugar Technology, Beet and Cane Sugar Manufacture. 1st ed. Berlin: Verlag; 1998. 1118 p. DOI: 10.36961/st
- [7] van Asselt AJ, Weeks MG. Dairy processing. In: *Sustainable Dairy Production*. 1st ed. Chichester: Wiley; 2013. p. 87-118. DOI: 10.1002/9781118489451.ch5
- [8] Anonymous. Meat Processing. In: *Meat Industry Guide*. London: UK Food Std. Agency; 2015. p. 1-36. Available from: https://webarchive.nationalarchives.gov.uk/20191202184215/https://www.food.gov.uk/sites/default/files/media/document/chapter15-meat-processing-final_version-2_0.pdf
- [9] Corbo MR, Bevilacqua A, Petruzzzi L, Casanova FP, Sinigaglia M. Functional Beverages: The Emerging Side of Functional Foods: Commercial Trends, Research, and Health Implications. *Compr Rev Food Sci Food Saf*. 2014;13:1192-206. DOI: 10.1111/1541-4337.12109
- [10] Wu Y, Yan B, Zhou J, Lian H, Yu X, Zhao J, et al. Effects of sourdough on improving the textural characteristics of microwave-steamed cake: A perspective from dielectric properties and water distribution. *J Food Sci*. 2020;85:3282-3292. DOI: 10.1111/1750-3841.15424
- [11] Bamforth CW, Cook DJ. Yoghurt and Other Fermented Milk Products. In: *Food, Fermentation, and Micro-organisms*. 2nd ed. Hoboken: Wiley; 2019. p. 183-186. DOI: 10.1002/9781119557456.ch11
- [12] Behare P, Kumar H, Mandal S. Yogurt: Yogurt Based Products. In: *Encyclopedia of Food and Health*. 1st ed. London: Elsevier; 2015. p. 625-631. DOI: 10.1016/B978-0-12-384947-2.00767-4
- [13] Kesenkaş H, Gürsoy O, Özbaş H. Kefir. In: *Fermented Foods in Health and Disease Prevention*. 1st ed. London: Elsevier; 2017. p. 339-361. DOI: 10.1016/B978-0-12-802309-9.00014-5
- [14] Prado MR, Blandón LM, Vandenberghe LPS, Rodrigues C, Castro GR, Thomaz-Soccol V, et al. Milk kefir: Composition, microbial cultures, biological activities, and related products. *Front Microbiol*. 2015;6:1-10. DOI: 10.3389/fmicb.2015.01177
- [15] Lager T. The Development and Manufacturing of Beer — An

- Introduction and Background for the Process-Industrial Illustrative Case. In: Contemporary Quality Function Deployment for Product and Process Innovation. 1st ed. London: World Scientific Publishing Company; 2019. p. 23-36. DOI: 10.1142/9789813279889_0002
- [16] Pozo-Bayón MA, Moreno-Arribas M V. Sherry Wines: Manufacture, Composition and Analysis. In: Encyclopedia of Food and Health. 2015. 1st ed. London: Elsevier; 2015. p. 779-784. DOI: 10.1016/B978-0-12-384947-2.00626-7
- [17] Gupta A, Verma JP. Sustainable bio-ethanol production from agro-residues: A review. *Renew Sustain Energy Rev.* 2015;41:550-567. DOI: 10.1016/j.rser.2014.08.032
- [18] O'Hara IM, Mundree SG, editors. Sugarcane-based biofuels and bioproducts. Sugarcane-based Biofuels and Bioproducts. 1st ed. Chichester: Wiley; 2016. 386 p. DOI:10.1002/9781118719862
- [19] Garcia-Parrilla MC, Torija MJ, Mas A, Cerezo AB, Troncoso AM. Vinegars and Other Fermented Condiments. In: Frias J, Martinez-Villaluenga C, Peñas E, editors. Fermented Foods in Health and Disease Prevention. 1st ed. London: Elsevier; 2017. p. 577-591. DOI: 10.1016/B978-0-12-802309-9.00025-X
- [20] Bekatorou A. Advances in Vinegar Production. 1st ed. Boca Raton: CRC Press. 2019. 522 p. DOI: 10.1201/9781351208475
- [21] Rogers P, Chen JS, Zidwick MJ. Organic acid and solvent production: Acetic, lactic, gluconic, succinic, and polyhydroxyalkanoic acids. In: Dworkin M, Falkow S, Rosenberg E, Schleifer KH, Stackebrandt E, editors. The Prokaryotes: Applied Bacteriology and Biotechnology. New York: Springer; 2014. p. 3-75. DOI: 10.1007/0-387-30741-9_19
- [22] Singh R, Mittal A, Kumar M, Mehta PK. Organic acids: An overview on microbial production. *Int J Adv Biotechnol Res.* 2017;8(1):104-111.
- [23] Ciriminna R, Meneguzzo F, Delisi R, Pagliaro M. Citric acid: Emerging applications of key biotechnology industrial product. *Chem Cent J.* 2017;11(22):1-9. DOI: 10.1186/s13065-017-0251-y
- [24] Gasca-González R, Prado-Rubio OA, Gómez-Castro FI, Fontalvo-Alzate J, Pérez-Cisneros ES, Morales-Rodriguez R. Techno-economic analysis of alternative reactive purification technologies in the lactic acid production process. In: Kiss A, Zondervan E, Lakerveld R, Özkan L, editors. 29th European Symposium on Computer Aided Process Engineering. Computer Aided Chemical Engineering. vol. 46. London: Elsevier; 2019. p. 457-462. DOI: 10.1016/B978-0-12-818634-3.50077-1
- [25] Srivastava N, Mishra PK, Upadhyay SN. Microbial cellulase production. In: Srivastava N, Mishra PK, Upadhyay SN, editors. Industrial Enzymes for Biofuels Production. 1st ed. London: Elsevier; 2020. p. 19-35. DOI: 10.1016/b978-0-12-821010-9.00002-4
- [26] Vargas M, Niehus X, Casas-Godoy L, Sandoval G. Lipases as biocatalyst for biodiesel production. *Methods Mol Biol.* 2018; 1835: 377-390. DOI: 10.1007/978-1-4939-8672-9_21
- [27] Mohanan N, Satyanarayana T. Amylases. In: Schmidt, T, editor. Encyclopedia of Microbiology. 4th ed. London: Academic Press; 2019. p. 107-126. DOI: 10.1016/B978-0-12-809633-8.13003-1
- [28] Trujillo-Toledo LE, García DM, Cruz EP, Intriago LMR, Pérez JN,

- Pais-Chanfrau JM. Fructosyltransferases and invertases: Useful enzymes in the food and feed industries. In: Kuddus M, editor. *Enzymes in Food Biotechnology: Production, Applications, and Future Prospects*. 1st ed. London: Academic Press; 2018. p. 451-469. DOI: 10.1016/B978-0-12-813280-7.00026-8
- [29] Flores-Maltos DA, Mussatto SI, Contreras-Esquivel JC, Rodríguez-Herrera R, Teixeira JA, Aguilar CN. Biotechnological production and application of fructooligosaccharides. *Crit Rev Biotechnol*. 2016;36:259-267. DOI: 10.3109/07388551.2014.953443
- [30] Pérez Cruz ER, Hernández García L, Martínez García D, Trujillo Toledo LE, Menéndez Rodríguez, Carmen, et al. Method for obtaining 1-kestose. Cuba; WO2014044230 A1, 2014. p. 12. Available from: <https://www.google.com/patents/WO2014044230A1?cl=en>
- [31] Fischer C, Kleinschmidt T. Synthesis of galactooligosaccharides using sweet and acid whey as a substrate. *Int Dairy J*. 2015;48:15-22. DOI: 10.1016/j.idairyj.2015.01.003
- [32] Pais-Chanfrau JM, Núñez-Pérez J, Espin-Valladares R del C, Lara-Fiallos MV, Trujillo-Toledo LE. Bioconversion of Lactose from Cheese Whey to Organic Acids. In: Gutiérrez-Méndez N, editor. *Lactose and Lactose Derivatives*. 1st ed. London: IntechOpen; 2020. p. 53-74. DOI: 10.5772/intechopen.92766
- [33] Lipták BG. *Optimization of Industrial Unit Processes*. 2nd ed. Boca Raton: CRC Press; 2020. 432 p. DOI: 10.1201/9780138744847
- [34] Lahiri SK. Optimization of Industrial Processes and Process Equipment. In: Lahiri SK, editor. *Profit Maximization Techniques for Operating Chemical Plants*. 1st ed. NJ: Wiley; 2020. p. 131-158. DOI: 10.1002/9781119532231.ch8
- [35] Jones B, Hunter JS, Montgomery DC. Partial replication of definitive screening designs. *Qual Eng*. 2020;32:1-6. DOI: 10.1080/08982112.2019.1680847
- [36] Montgomery DC, Runger GC. Design of experiment with several factors. In: Montgomery DC, Runger GC, editors. *Applied Statistics and Probabilities for Engineers*. 7th ed. Hoboken: Wiley; 2018. p. 375-433.
- [37] Montgomery DC. *Design and analysis of experiments*. 9th ed. Hoboken: Wiley; 2017. 748 p.
- [38] Myers RH, Montgomery DC, Geoffrey Vining G, Borror CM, Kowalski SM. *Response Surface Methodology: A Retrospective and Literature Survey*. *Journal of Quality Technology*. 2003;36:53-78. DOI: 10.1080/00224065.2004.11980252
- [39] Khuri AI, Mukhopadhyay S. *Response surface methodology*. Wiley Interdisciplinary Reviews: Computational Statistics. 2010;2:128-149. DOI: 10.1002/wics.73
- [40] Bezerra MA, Santelli RE, Oliveira EP, Villar LS, Escalera LA. Response surface methodology (RSM) as a tool for optimization in analytical chemistry. *Talanta*. 2008;76: 965-977. DOI: 10.1016/j.talanta.2008.05.019
- [41] Manojkumar N, Muthukumaran C, Sharmila G. A comprehensive review on the application of response surface methodology for optimization of biodiesel production using different oil sources. *Journal of King Saud University - Engineering Sciences*. DOI: 10.1016/j.jksues.2020.09.012
- [42] Yolmeh M, Jafari SM. Applications of Response Surface Methodology in the Food Industry Processes. *Food and Bioprocess Technology*. 2017;10:413-433. DOI: 10.1007/s11947-016-1855-2

- [43] Granato D, de Araújo Calado VÔM, Jarvis B. Observations on the use of statistical methods in Food Science and Technology. Food Res. Inter. 2014;55:137-149. DOI: 10.1016/j.foodres.2013.10.024
- [44] O'Neill CM, Cruz-Romero MC, Duffy G, Kerry JP. The application of response surface methodology for the development of sensory accepted low-salt cooked ham using high pressure processing and a mix of organic acids. Innov Food Sci Emerg Technol. 2018;45:401-411. DOI: 10.1016/j.ifset.2017.12.009
- [45] Dastras M, Soltanzadeh M, Peighambaroust SH. Production of cereal-based probiotic beverage optimized by response surface methodology and investigation of its properties. Iran J Nutr Sci Food Technol. 2019;14: 47-56.
- [46] Yih Hui B, Mohamad Zain NN, Mohamad S, Varanusupakul P, Osman H, Raoov M. Poly (cyclodextrin-ionic liquid) based ferrofluid: A new class of magnetic colloid for dispersive liquid phase microextraction of polycyclic aromatic hydrocarbons from food samples prior to GC-FID analysis. Food Chem. 2020;314:126214. DOI: 10.1016/j.foodchem.2020.126214
- [47] Hesam F, Tarzi BG, Honarvar M, Jahadi M. Pistachio (*Pistacia vera*) shell as a new candidate for enzymatic production of xylooligosaccharides. J Food Meas Charact. 2021;15:33-41. DOI: 10.1007/s11694-020-00594-y
- [48] Nadeem F, Mehmood T, Naveed M, Shamas S, Saman T, Anwar Z. Protease Production from *Cheotomium globusum* Through Central Composite Design Using Agricultural Wastes and Its Immobilization for Industrial Exploitation. Waste and Biomass Valorization. 2020;11:6529-6539. DOI: 10.1007/s12649-019-00890-9
- [49] Zamri AI, Latiff NF, Abdullah QH, Ahmad F. Extraction and optimization of chitosan from razor clam (*Ensis arcuatus*) shells by using response surface methodology (RSM). Food Res. 2020;4:674-678. DOI: 10.26656/fr.2017.4(3).308
- [50] Hesam F, Tarzi BG, Honarvar M, Jahadi M. Valorization of sugarcane bagasse to high value-added xylooligosaccharides and evaluation of their prebiotic function in a synbiotic pomegranate juice. Biomass Convers Biorefinery. DOI: 10.1007/s13399-020-01095-0
- [51] Kalathinathan P, Kodiveri Muthukaliannan G. A statistical approach for enhanced production of β -galactosidase from *Paracoccus sp.* and synthesis of galacto-oligosaccharides. Folia Microbiol (Praha). 2020;65:811-822. DOI: 10.1007/s12223-020-00791-8
- [52] Israni N, Venkatachalam P, Gajaraj B, Varalakshmi KN, Shivakumar S. Whey valorization for sustainable polyhydroxyalkanoate production by *Bacillus megaterium*: Production, characterization and in vitro biocompatibility evaluation. J Environ Manage. DOI: 10.1016/j.jenvman.2019.109884
- [53] Moyo LB, Iyuke SE, Muvhiiwa RF, Simate GS, Hlabangana N. Application of response surface methodology for optimization of biodiesel production parameters from waste cooking oil using a membrane reactor. South African J Chem Eng. 2021;35:1-7. DOI: 10.1016/j.sajce.2020.10.002
- [54] Kalagatur NK, Kamasani JR, Siddaiah C, Gupta VK, Krishna K, Mudili V. Combinational Inhibitory Action of *Hedychium spicatum* L. Essential Oil and γ -Radiation on Growth Rate and Mycotoxins Content of *Fusarium graminearum* in Maize: Response Surface Methodology. Front

Microbiol. 2018;9:1511. DOI: 10.3389/fmicb.2018.01511

[55] Kainthola J, Kalamdhad AS, Goud V V. Optimization of process parameters for accelerated methane yield from anaerobic co-digestion of rice straw and food waste. *Renew Energy*. 2020;149: 1352-1359. DOI: 10.1016/j.renene.2019.10.124

[56] Parra-Orobio BA, Torres-López WA, Torres-Lozada P. Response Surface Methodology as an Optimization Tool for Anaerobic Digestion of Food Waste. *Water Air Soil Pollut.* 2020;231:385. DOI: 10.1007/s11270-020-04764-y

[57] Kucharczyk K, Zyla K, Tuszyński T. Control of selected fermentation indices by statistically designed experiments in industrial scale beer fermentation. *Czech J Food Sci.* 2020;38:330-336. DOI: 10.17221/291/2019-CJFS

[58] Abhilasha P, Pal US. Effect of Ohmic Heating on Quality and Storability of Sugarcane Juice. *Int J Curr Microbiol Appl Sci.* 2018;7:2856-2868. DOI: 10.20546/ijcmas.2018.701.340

[59] Németh, Jánosi SZ. Extraction of steviol glycosides from dried *Stevia rebaudiana* by pressurized hot water extraction. *Acta Aliment.* 2019;48:241-252. DOI: 10.1556/066.2019.48.2.12

[60] Pui LP, Karim R, Yusof YA, Wong CW, Ghazali HM. Optimization of spray-drying parameters for the production of 'Cempedak' (*Artocarpus integer*) fruit powder. *J Food Meas Charact.* 2020;14:1-12. DOI: 10.1007/s11694-020-00565-3

[61] Armstrong L, Araújo Vieira do Carmo M, Wu Y, Antônio Esmerino L, Azevedo L, Zhang L, et al. Optimizing the extraction of bioactive compounds from pu-erh tea (*Camellia sinensis var. assamica*) and evaluation of antioxidant, cytotoxic, antimicrobial, antihemolytic,

and inhibition of α -amylase and α -glucosidase activities. *Food Res Int.* 2020;137(109430). DOI: 10.1016/j.foodres.2020.109430

[62] Unuofin JO, Okoh AI, Nwodo UU. Maize stover as a feedstock for enhanced laccase production by two gammaproteobacteria: A solution to agroindustrial waste stockpiling. *Ind Crops Prod.* 2019;129: 611-623. DOI: 10.1016/j.indcrop.2018.12.043

[63] Shruthi VH, Hiregoudar S, Nidoni U. Evaluation of textural properties of corn based extruded products. *Plant Arch.* 2019;19:2405-2410. Available from: [http://plantarchives.org/19-2/2405-2410\(5310\).pdf](http://plantarchives.org/19-2/2405-2410(5310).pdf)

[64] Abdulhadi Y, Ashish V. Response Surface Methodology approach for optimization of endoglucanase from alkaliphilic *Fusarium oxysporum* VSTPDK and its potential application in pulp and paper industry. *Res J Biotechnol.* 2021;16(1):62-67.

[65] Dionisio AP, de Carvalho-Silva LB, Vieira NM, Wurlitzer NJ, Pereira AC da S, Borges M de F, et al. Antioxidant and prebiotic effects of a beverage composed by tropical fruits and yacon in alloxan-induced diabetic rats. *Food Sci Technol.* 2020;40:202-208. DOI: 10.1590/fst.34518

[66] Leong CY, Chua LS. Optimization of concentrating process using rotary vacuum evaporation for pineapple juice. *Chem Eng Trans.* 2020;78:7-12. Available from: <https://www.aidic.it/cet/20/78/002.pdf>

[67] Deveci EÜ, Gönen Ç, Akarsu C. Pre-treatment optimization of barley straw as agro-industrial waste via alkaline peroxide and ultrasound for soluble sugar production and degradation. *Biomass Convers Biorefinery.* 2020;10:1-9. DOI: 10.1007/s13399-020-00879-8

- [68] Solarte-Toro JC, Romero-García JM, Susmozas A, Ruiz E, Castro E, Cardona-Alzate CA. Techno-economic feasibility of bioethanol production via biorefinery of olive tree prunings (OTP): Optimization of the pretreatment stage. *Holzforschung*. 2019;73:3-13. DOI: 10.1515/hf-2018-0096
- [69] Bhat B, Vaid S, Habib B, Bajaj BK. Design of experiments for enhanced production of bioactive exopolysaccharides from indigenous probiotic lactic acid bacteria. *Indian J Biochem Biophys*. 2020;57(5):539-551.
- [70] Pais-Chanfrau JM, Toledo LET, Córdor PMA, Guerrero MJC, Pérez JN, Intriago LMR. Response surface methodology to optimize a bioprocess for kefir production. *La Prensa Medica Argentina*. 2018;104:1-5. DOI: 10.4172/0032-745X.1000285
- [71] Rivadeneira JP, Wu T, Ybanez Q, Dorado AA, Migo VP, Nayve FRP, et al. Microwave-assisted extraction of pectin from “Saba” banana peel waste: Optimization, characterization, and rheology study. *Int J Food Sci*. 2020;2020:1-9. DOI: 10.1155/2020/8879425
- [72] Kuo CH, Huang CY, Shieh CJ, Wang HMD, Tseng CY. Hydrolysis of Orange Peel with Cellulase and Pectinase to Produce Bacterial Cellulose using *Gluconacetobacter xylinus*. *Waste and Biomass Valorization*. 2019;10: 85-93. DOI: 10.1007/s12649-017-0034-7
- [73] Domingo CJA, De Vera WM, Pambid RC, Austria VC. Playing with the senses: application of Box-Behnken design to optimize the bukayo formulation. *Food Res*. 2019;3(6):833-839. DOI: 10.26656/fr.2017.3(6).190
- [74] Haq M, Pendleton P, Chun BS. Utilization of Atlantic Salmon By-product Oil for Omega-3 Fatty Acids Rich 2-Monoacylglycerol Production: Optimization of Enzymatic Reaction Parameters. *Waste and Biomass Valorization*. 2020;11:1-11. DOI: 10.1007/s12649-018-0392-9
- [75] Chan LG, Cohen JL, Ozturk G, Hennebelle M, Taha AY, De Moura Bell JMLN. Bioconversion of cheese whey permeate into fungal oil by *Mucor circinelloides*. *J Biol Eng*. 2018;12(25):1-14. DOI: 10.1186/s13036-018-0116-5
- [76] Tapia-Quirós P, Montenegro-Landívar MF, Reig M, Vecino X, Alvarino T, Cortina JL, et al. Olive mill and winery wastes as viable sources of bioactive compounds: A study on polyphenols recovery. *Antioxidants*. 2020;9(11):1-15. DOI: 10.3390/antiox9111074
- [77] Lakka A, Lalas S, Makris DP. Development of a low-temperature and high-performance green extraction process for the recovery of polyphenolic phytochemicals from waste potato peels using hydroxypropyl β -cyclodextrin. *Appl Sci*. 2020;10:1-12. DOI: 10.3390/app10103611
- [78] Liang Q, Liu Y, Chen M, Ma L, Yang B, Li L, et al. Optimized preparation of activated carbon from coconut shell and municipal sludge. *Mater Chem Phys*. 2020;241(2):122327. DOI: 10.1016/j.matchemphys.2019.122327
- [79] Vénica CI, Bergamini C V, Perotti MC. Response surface methodology as a tool for modelling galacto-oligosaccharide production. *J Dairy Res*. 2017;84:464-470. DOI: 10.1017/S0022029917000541
- [80] Deng Y, Xu M, Ji D, Agyei D. Optimization of β -galactosidase Production by Batch Cultures of *Lactobacillus leichmannii* 313 (ATCC 7830™). *Fermentation*. 2020;6:1-17. DOI: 10.3390/fermentation6010027
- [81] Teixeira RF, Benvenutti L, Burin VM, Gomes TM, Ferreira SRS,

- Zielinski AAF. An eco-friendly pressure liquid extraction method to recover anthocyanins from broken black bean hulls. *Innov Food Sci Emerg Technol*. 2021;67:1-8. DOI: 10.1016/j.ifset.2020.102587
- [82] Martins EH, Ratuchne A, de Oliveira Machado G, Knob A. Canola meal as a promising source of fermentable sugars: Potential of the *Penicillium glabrum* crude extract for biomass hydrolysis. *Biocatal Agric Biotechnol*. 2020;27:1-10. DOI: 10.1016/j.bcab.2020.101713
- [83] Carevic M, Banjanac K, Milivojevic A, Corovic M, Bezbradica D. Optimization of galacto-oligosaccharides synthesis using response surface methodology. *Food Feed Res*. 2017;44:1-10. DOI: 10.5937/ffr1701001c
- [84] Shi T, Lin J, Li J, Zhang Y, Jiang C, Lv X, et al. Pre-treatment of sugarcane bagasse with aqueous ammonia–glycerol mixtures to enhance enzymatic saccharification and recovery of ammonia. *Bioresour Technol*. 2019;289:1-9. DOI: 10.1016/j.biortech.2019.121628
- [85] Arumugam A, Anudakshaini TS, Shruthi R, Jeyavishnu K, Sundarra Harini S, Sharad JS. Low-cost production of PHA using cashew apple (*Anacardium occidentale* L.) juice as potential substrate: optimization and characterization. *Biomass Convers Biorefinery*. 2020;10:1-12. DOI: 10.1007/s13399-019-00502-5
- [86] Santosa FH, Laysandra L, Soetaredjo FE, Santoso SP, Ismadji S, Yuliana M. A facile noncatalytic methyl ester production from waste chicken tallow using single step subcritical methanol: Optimization study. *Int J Energy Res*. 2019;43:1-12. DOI: 10.1002/er.4844
- [87] Roy VC, Getachew AT, Cho YJ, Park JS, Chun BS. Recovery and bio-potentialities of astaxanthin-rich oil from shrimp (*Penaeus monodon*) waste and mackerel (*Scomberomorus niphonius*) skin using concurrent supercritical CO₂ extraction. *J Supercrit Fluids*. 2020;159:1-10. DOI: 10.1016/j.supflu.2020.104773
- [88] Mandik YI, Cheirsilp B, Srinuanpan S, Maneechote W, Boonsawang P, Prasertsan P, et al. Zero-waste biorefinery of oleaginous microalgae as promising sources of biofuels and biochemicals through direct transesterification and acid hydrolysis. *Process Biochem*. 2020;95:214-22. DOI: 10.1016/j.procbio.2020.02.011
- [89] Lee M, Yang M, Choi S, Shin J, Park C, Cho SK, et al. Sequential production of lignin, fatty acid methyl esters and biogas from spent coffee grounds via an integrated physicochemical and biological process. *Energies*. 2019;12:1-13. DOI: 10.3390/en12122360
- [90] Ali B, Yusup S, Quitain AT, Bokhari A, Kida T, Chuah LF. Heterogeneous catalytic conversion of rapeseed oil to methyl esters: Optimization and kinetic study. In: Hosseini M, editor. *Advances in Feedstock Conversion Technologies for Alternative Fuels and Bioproducts: New Technologies, Challenges and Opportunities*. 1st ed. London: Elsevier; 2019. p. 221-38. DOI: 10.1016/B978-0-12-817937-6.00012-6
- [91] Ubando AT, Felix CB, Chen WH. Biorefineries in circular bioeconomy: A comprehensive review. *Bioresour Technology*. 2020; 299:122585. DOI: 10.1016/j.biortech.2019.122585
- [92] Imbert E. Food waste valorization options: Opportunities from the bioeconomy. *Open Agric*. 2017;2:195-204. DOI: 10.1515/opag-2017-0020
- [93] Dahiya S, Kumar AN, Shanthi Sravan J, Chatterjee S, Sarkar O,

Mohan SV. Food waste biorefinery: Sustainable strategy for circular bioeconomy. *Bioresource Technology*. 2018;248:2-12. DOI: 10.1016/j.biortech.2017.07.176

2019;10:631-640. DOI: 10.1007/s12649-018-0240-y

[94] Pais-Chanfrau J, Núñez-Pérez J, Lara-Fiallos M, Rivera-Intriago L, Abril V, Cuaran-Guerrero M, et al. Milk Whey- From a Problematic Byproduct to a Source of Valuable Products for Health and Industry: An Overview from Biotechnology. *La Prensa Medica Argentina*. 2017;103(4):1-11. DOI: 10.4172/lpma.1000254

[100] Katakotwala R, Naresh Kumar A, Chakraborty D, Mohan SV. Valorization of sugarcane waste: Prospects of a biorefinery. In: Vara Prasad N, de Campos Fava PJ, Vithanage M, Mohan SV, editors. *Industrial and Municipal Sludge: Emerging Concerns and Scope for Resource Recovery*. 1st ed. London: Elsevier; 2019. p. 47-60. DOI: 10.1016/B978-0-12-815907-1.00003-9

[95] Bosco F, Carletto RA, Marmo L. An integrated cheese whey valorization process. *Chem Eng Trans*. 2018;64:379-384. DOI: 10.3303/CET1864064

[96] Lappa IK, Papadaki A, Kachrimanidou V, Terpou A, Koulougliotis D, Eriotou E, et al. Cheese whey processing: Integrated biorefinery concepts and emerging food applications. *Foods*. 2019;8:1-37. DOI: 10.3390/foods8080347

[97] Martinez-Hernandez E, Amezcua-Allieri MA, Sadhukhan J, Anell JA. Sugarcane Bagasse Valorization Strategies for Bioethanol and Energy Production. In: de Oliveira AB, editor. *Sugarcane - Technology and Research*. 1st ed. London: IntechOpen; 2018. p. 71-83. DOI: 10.5772/intechopen.72237

[98] Guna V, Ilangovan M, Hu C, Venkatesh K, Reddy N. Valorization of sugarcane bagasse by developing completely biodegradable composites for industrial applications. *Ind Crops Prod*. 2019;131:25-31. DOI: 10.1016/j.indcrop.2019.01.011

[99] Ozdal M, Kurbanoglu EB. Citric Acid Production by *Aspergillus niger* from Agro-Industrial By-Products: Molasses and Chicken Feather Peptone. *Waste and Biomass Valorization*.